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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,342	12/31/2003	Jeffry G. Weers	0190.00	7605

21968 7590 02/06/2008

NEKTAR THERAPEUTICS
201 INDUSTRIAL ROAD
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EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/751,342	WEERS ET AL.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,23-25,28-31,34-40,63-78 and 97* is/are pending in the application.

4a) Of the above claim(s) *97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,23-25,28-31,34-40 and 63-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of November 13, 2007 made to the office action filed June 14, 2007. Claims 1-20, 23-25, 28-31, 34-40, 63-78 and 97 are pending. Claims 1, 23 and 63 are amended and claims 21, 22, 26, 27, 32, 33, 41-62 and 79-96 are cancelled. Claims 97 is withdrawn.

In light of the amendments and cancellation of claims, the following rejections are withdrawn: 1) 35 U.S.C. 102(e) rejection of claims 1-7, 11-21, 23-29, 33-41, 43 and 45-53 as being anticipated by Tarara et al.; 2) 35 U.S.C. 103(a) rejection of claims 21 and 41 as being unpatentable over Ponikau as applied to claims 1-15, 20, 23-35, 40 and 43-52 above in view of Johnson; and 3) 35 U.S.C. 103(a) rejection of claims 22 and 42 as being unpatentable over Ponikau as applied to claims 1-15, 20, 23-35, 40 and 43-52 above in view of Lloyd et al.

The Applicant's arguments of the 35 U.S.C. 103(a) rejection of claims 8-10, 30-32 and 44 as being unpatentable over Tarara et al. were found persuasive, and thus withdrawn. Particularly, the Applicant has established common ownership and thus the reference can not be used as a reference under 35 U.S.C. 103(a).

The Examiner acknowledges Applicant's indication that a terminal disclaimer will be filed upon identification of allowable subject matter to obviate the provisional

obviousness-type double patenting rejection over U.S. Patent Application No. 11/187,757. However, as such terminal disclaimers have not as-yet been filed, the provisional obviousness-type double patenting rejections over these co-pending applications are being maintained.

For the reasons in the previous office action and below, the Applicant's arguments of the following rejections were found not persuasive, thus the rejections are maintained: 1) 35 U.S.C. 112, first paragraph rejection of claims 1-96; 2) 35 U.S.C. 103(a) rejection of claims 1-15, 23-35 and 43-52 as being unpatentable over Ponikau; and 3) 35 U.S.C. 103(a) rejection of claims 17-19 and 37-39 as being unpatentable over Ponikau as applied to claims 1-15, 23-35 and 43-52 above in view of Unger.

Due to the amendment and cancellation to the claims, the modified 35 U.S.C. 103(a) rejections are made below. Due to the Applicant establishing common ownership of the Weickert et al. reference, the reference can not be used as a reference under 35 U.S.C. 103(a). Thus, a new rejection is made below and therefore provides for a new Non-Final rejection.

The Applicant's arguments are addressed below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 18-20, 23-25, 28-31, 34-36, 38-40, and 63-72 and 74-76 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-25, 27-30, 35-44 of copending Application No. 11/187,757 ('757). Although the conflicting claims are not identical, they are not patentably distinct from each other. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Application '757 teaches a method for treating a patient suffering from a fungal infection of the lung, comprising administering to the patient a therapeutically effective amount of a pharmaceutical formulation comprising a lipid matrix and at least one particle of an antifungal agent in the lipid matrix wherein the aerosolized (see claim 35) pharmaceutical formulation is for pulmonary administration (see claim 45) via inhalation (see claims 23 and 27). For clarification, the application '757 defines treating as providing prevention of a particular condition (see page 2, paragraph 26, lines 6-8). The lipid matrix comprises a phospholipid (see claim 7). The composition can be a dry powder that has a bulk density of less than 0.5 g/cm^3. The antifungal agent is amphotericin B (see claims 29 and 30). The amount of antifungal agent is at least twice the minimum inhibitory concentration of the antifungal agent for at least one week (see claim 35), three weeks or three months (see claims 39-42). Thus, determining the minimum inhibitory concentration is taught in application '757 because in order to administer twice the minimum inhibitory concentration, the minimum inhibitory concentration of the antifungal agent needs to be determined. The minimum inhibitory concentration is in the epithelial lining or the solid tissue of the lung (see claims 36 and 37), with a lung concentration at least 9 μg/g or in the range of 9 μg/g to 15 μg/g (see claims 43 and 44).

The application '757 does not teach a single dose or two doses of the pharmaceutical formulation during the first week of administration (applicant's claims 8 and 9). The two period administration wherein the antifungal agent is administered

more frequently or at a higher dosage during the first period than during the second period is also not taught (see applicant's claims 10). Neither is the administration comprising delivering the formulation periodically to maintain the antifungal agent lung concentration taught (see applicant's claim 13).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of '757 and the administration detailed above in the applicant's claims 8, 9, 10 and 13 and determining the minimum inhibitory concentration of an antifungal agent for inhibiting pulmonary fungal growth because of the following: (1) the antifungal agent is administered for at least one week, three weeks or three months to maintain the twice the minimum inhibitory concentration (see claims 35 and 40); (2) it is within the art to administer a drug several times during a treatment. In order to treat the fungal infection the antifungal agent must be present in concentrations that are effective. Whether the drug is administered once, twice, or several times, the important factor is that twice the minimum inhibitory concentration is maintained in the lungs.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20, 23-25, 28-31, 34-40 and 63-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a pulmonary fungal infection , does not reasonably provide enablement for preventing a pulmonary fungal infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating and/or providing prophylaxis against a pulmonary fungal infection. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method of treating and/or providing prophylaxis against a pulmonary fungal infection, the method comprising: determining the minimum inhibitory concentration of an antifungal agent for inhibiting pulmonary fungal growth; and administering a aerosolized pharmaceutical formulation comprising the antifungal agent to the lungs of a patient; wherein a sufficient amount of the pharmaceutical formulation is administered to maintain for at least one week a target antifungal agent lung concentration of at least two times the determined minimum inhibitory concentration."

(2) The breadth of the claims:

Claims 1-20, 23-25, 28-31, 34-40 and 63-78 embraces preventing pulmonary fungal infection. This reads on completely preventing all pulmonary fungal infections. The specification does not enable the complete prevention of pulmonary fungal infections.

(3) The state of the prior art:

The state of the art regarding preventing pulmonary fungal infections is very low or do not exist.

(4) The predictability or unpredictability of the art:

The predictability of completely preventing pulmonary fungal infections is relatively low. Therefore, to one skilled in the art, prevention of pulmonary fungal infections is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the prevention of pulmonary fungal infections is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that completely prevent pulmonary fungal infections. The specification states that the pharmaceutical formulation administered prophylactically comprising an antifungal agent is to reduce the likelihood of developing a fungal infection during an immunocomprised period (see page 11, lines 17-21). Reduction in the likelihood of developing a fungal infection does not provide complete prevention from an infection. One would need to show data that supported a patient never developed a fungal infection after administering the applicant's method. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on the complete prevention of all pulmonary fungal infections. As discussed above the specification fails to provide any support for completely preventing pulmonary fungal infections. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating pulmonary fungal infections, but not for preventing pulmonary fungal infections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 1-15, 23-25, 28-31, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ponikau (US 6,207,703 B1).

Ponikau teaches a pharmaceutical composition for treating an immune response to fungus in a mammal or a fungal related condition in the pulmonary anatomy comprising an effective dose of an anti-fungal agent (see column 10, lines 42, 43, 50-55) such as amphotericin B (see column 4, line 55 and claim 19) in an aerosol form as a powder or solution (see column 3, lines 65, 66 and column 4, lines 1; addresses claims 1, 11, 15 and 20-23). The formulation contains about 0.01 ng to about 1000 mg of the antifungal agent (see column 4, lines 10-12; addresses claims 12-14, 23 and 34). The effective amount of a formulation can change or remain the same during an effective duration. The effective frequency of direct mucoadministration can be from about four times a day to about once every other week in some embodiments of the invention, or about twice a day in still other embodiments of the invention. In addition the effective frequency of direct mucoadministration can be greater than once a day, or greater than once a week. The effective duration can be greater than about 7, 14, 30, 60, 90 days (see column 4, lines 28-38; addresses claims 1-10, 23 and 28-31) or can vary from several days to several weeks, months or years (see column 25, lines 43 and 44). A

typical effective amount can be any amount greater than or equal to the minimum inhibitory concentration for the fungal organism, and such amounts can be determined for individual antifungal agents using commonly available or easily ascertainable information involving antifungal effectiveness concentrations (see column 24, lines 10-12 and lines 21-23; addresses claims 1 and 23). Direct mucoadministration to the lung airways can include inhalations or nasal sprays provided that the administered agent contacts lung airway mucus prior to crossing epithelium (see column 28, lines 9-12; addresses claims 1 and 23). Any device can be used to administer the agent to the lung airway including inhaler, nebulizer, aerosol canister, spray can, and mask (see column 28, lines 17-20).

Ponikau does not specifically teach that the minimum inhibitory concentration is in the epithelial lining or the solid tissue of the lung (claims 2, 3, 24 and 25).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Ponikau and the minimum inhibitory concentration is in the epithelial lining or the solid tissue of the lung because Ponikau teaches the following: (1) direct mucoadministration to the lung airways or pulmonary anatomy can include inhalations or nasal sprays provided that the administered agent contacts lung airway mucus prior to crossing epithelium (see column 28, lines 9-12 and see column 10, lines 42, 43, 50-55); and (2) a typical effective amount can be any amount greater than or equal to the minimum inhibitory concentration for the fungal

organism, and such amounts can be determined for individual antifungal agents using commonly available or easily ascertainable information involving antifungal effectiveness concentrations (see column 24, lines 10-12 and lines 21-23).

(2) Claims 16-20 and 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ponikau (US 6,207,703 B1) as applied to claims 1-15, 23-25, 28-31, 34 and 35 above in view of Straub et al. (US 6,395,300 B1).

Ponikau teachings are as applied to claims 1-15, 23-25, 28-31, 34 and 35 above.

Ponikau does not teach a bulk density of less than 0.5 g/cm^3 (claims 16 and 36), a dry formulation (claims 20 and 40), wherein the pharmaceutical formulation comprises hollow and/or porous particles (claims 17 and 37), wherein the pharmaceutical formulation further comprises a matrix material that comprises one or more phospholipids (claims 18, 19, 38 and 39).

Straub et al. teaches low aqueous solubility drugs such as the anti-fungal drug amphotericin B in a porous matrix form to provide a faster rate of dissolution following administration to a patient, as compared to non-porous matrix forms of the drug (see abstract, lines 1-2 and 15-18 and column 4, lines 47-48). The preferred embodiment is for oral administration using a dry powder inhaler for pulmonary administration (see

column 3, lines 1 and 6-8). The matrix further includes a pegylated excipient, such as pegylated phospholipic to shield the drug from macrophage uptake, which prolongs its half-life or enhance bioavailability of the drug (see column 2, lines 63-67). The density of the dry porous matrix powder is preferably less than 0.8 g/mL to provide sufficient surface area to enhance wetting of the dry porous matrix and enhance drug dissolution (see column 3, lines 65-66 and column 4, lines 2-5).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Ponikau and a bulk density of less than 0.5 g/cm^3, a dry formulation, and wherein the pharmaceutical formulation comprises hollow and/or porous particles within a matrix material that comprises one or more phospholipids because Straub et al. teaches the following: (1) drugs such as the anti-fungal drug amphotericin B in a porous matrix form to provide a faster rate of dissolution following administration to a patient, as compared to non-porous matrix forms of the drug (see abstract, lines 1-2 and 15-18 and column 4, lines 47-48); (2) the density of the dry porous matrix powder is preferably less than 0.8 g/mL to provide sufficient surface area to enhance wetting of the dry porous matrix and enhance drug dissolution (see column 3, lines 65-66 and column 4, lines 2-5); and (3) the matrix further includes a pegylated excipient, such as pegylated phospholipic to shield the drug from macrophage uptake, which prolongs its half-life or enhance bioavailability of the drug (see column 2, lines 63-67). Thus, it would be beneficial for the methods and compositions of Ponikau to be dry, have a specific bulk density, and wherein the

pharmaceutical formulation comprises hollow and/or porous particles within a matrix material that comprises one or more phospholipids because of the reasons stated above.

(3) Claims 17-19 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ponikau (US 6,207,703 B1) as applied to claims 1-15, 20, 23-35, 40, and 43-52 above in view of Unger (US 2001/0018072 A1).

Ponikau teachings are as applied to claims 1-15, 20, 23-35, 40, and 43-52 above.

Ponikau does not teach hollow and/or porous particles or a matrix material that comprises one or more phospholipids.

Unger teaches a solid porous matrix comprising a surfactant, such as phospholipids (see page 2, paragraph 19, lines 6 and 8) in combination with a bioactive agent (see abstract, lines 1 and 2), such as antifungal agents amphotericin B (see page 16, column 1, lines 19-21 and claim 27). The composition can be applied pulmonarily via inhalation by delivery of an aerosol (see page 35, paragraph 291, lines 13, 14, and 16). The invention is useful in delivering bioactive agents to a patient's lungs (see page 36, paragraph 297, lines 1 and 2).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Ponikau and a matrix material that comprises one or more phospholipids because Unger teaches the following: (1) a solid porous matrix comprising a surfactant, such as phospholipids (see page 2, paragraph 19, lines 6 and 8) in combination with a bioactive agent (see abstract, lines 1 and 2), such as antifungal agents amphotericin B (see page 16, column 1, lines 19-21 and claim 27); and (2) The invention is useful in delivering bioactive agents to a patient's lungs (see page 36, paragraph 297, lines 1 and 2).

Response to Arguments

Applicant's arguments with respect to all cancelled and amended claims have been considered but are moot in view of the new ground(s) of rejection.

35 U.S.C. 112 rejection

> The Applicant argues that the amended claims to read on administering directly to the lungs by inhalation properly reads on treatment to any patient in need of such treatment. Moreover, one skilled in the art would readily be able to perform the steps of ascertaining the type of pulmonary fungal infection, selecting an antifungal known to be efficacious against the infection and selecting a dose and regimen to treat said infection.

The Examiner disagrees because the claim terminology "prophylaxis" reads on the complete prevention of fungal infections. Thus, a patient following the Applicant's

method would never be infected by any type of pulmonary, which is not enabled by the current specification. The Examiner recommends removing the term "prophylaxis" and provide a method of treatment.

35 U.S.C. 103(a) over Ponikau et. al.

> The Applicant argues that Ponikau et al. is limited to teaching a method and materials for treating a non-invasive fungus induced rhinosinusitis, and has nothing to do with pulmonary fungus or pulmonary delivery and in particular does not teach or suggest methods and formulations comprising powder for pulmonary delivery. The Applicant further argues that the claimed invention must be considered as a whole, the references must be considered as a whole and suggest the desirability and obviousness of making the combination, and the references must be viewed without the benefit of hindsight.

The Examiner disagrees because Ponikau et al. teaches a pharmaceutical composition for treating an immune response to fungus in a mammal or a fungal related condition in the pulmonary anatomy comprising an effective dose of an anti-fungal agent (see column 10, lines 42, 43, 50-55) such as amphotericin B (see column 4, line 55 and claim 19) in an aerosol form as a powder or solution (see column 3, lines 65, 66 and column 4, lines 1; addresses claims 1, 11, 15 and 20-23). A typical effective amount can be any amount greater than or equal to the minimum inhibitory concentration for the fungal organism, and such amounts can be determined for individual antifungal agents using commonly available or easily ascertainable information involving antifungal effectiveness concentrations (see column 24, lines 10-12 and lines 21-23; addresses

claims 1 and 23). Any device can be used to administer the agent to the lung airway including inhaler, nebulizer, aerosol canister, spray can, and mask (see column 28, lines 17-20). Thus, Ponikau et al. obviously teaches the Applicant's claimed invention. The obviousness of the Ponikau et al. reference is in light of Ponikau not specifically teaching that the minimum inhibitory concentration is in the epithelial lining or the solid tissue of the lung (claims 2, 3, 24 and 25). The obviousness is taught by Ponikau et al. by the following teachings: (1) direct mucoadministration to the lung airways or pulmonary anatomy can include inhalations or nasal sprays provided that the administered agent contacts lung airway mucus prior to crossing epithelium (see column 28, lines 9-12 and see column 10, lines 42, 43, 50-55); and (2) a typical effective amount can be any amount greater than or equal to the minimum inhibitory concentration for the fungal organism, and such amounts can be determined for individual antifungal agents using commonly available or easily ascertainable information involving antifungal effectiveness concentrations (see column 24, lines 10-12 and lines 21-23). Therefore the Applicant's claimed invention and the reference is taken as a whole, and obviousness has been addressed. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the

applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

35 U.S.C. 103(a) over Ponikau et. al. in view of Unger

The Applicant argues that Unger teaches non-specifically delivery of active agents to a patent's lungs, a concept which is old in the art. Thus, either alone, or combined with Ponikau et al. does not teach, suggest or disclose applicants specifically claimed method of treatment.

The Examiner respectfully disagrees, and notes that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, Unger teaches a specific delivery in that the antifungal agents such as amphotericin B (see page 16, column 1, lines 19-21 and claim 27) can be applied pulmonarily via inhalation by delivery of an aerosol (see page 35, paragraph 291, lines 13, 14, and 16).

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose

telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KDC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER